AMENDMENT

In the Claims

4. (Amended) A method according to claim 3, wherein said first and second oligonucleotides bear different labels.

REMARKS

Claims 17-26 have been canceled. Claims 1-16 are pending. For the Examiner's convenience a copy of the currently pending claims is attached hereto. Claim 4 is amended; and a copy of the version showing changes made is attached hereto. Support for the amendment is found throughout the specification including claims 1-3. Favorable consideration of the following comments relative to the outstanding rejections as they may apply to the present claims is respectfully requested for the following reasons.

RESPONSE TO REJECTIONS

Response to Rejection Under 35 U.S.C. § 112 second paragraph

The Examiner rejects claim 4 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to point out and distinctly claim the subject matter of the invention. Specifically, the Examiner points to the limitation "different oligonucleotides" and maintains that it lacks sufficient antecedent basis. Applicants have amended Claim 4 to recite "said first and second oligonucleotides," thereby providing adequate antecedent basis. Support for this amendment can be found in claims 1-3 and elsewhere in the application. Thus, Applicants request the Examiner to withdraw the rejection.

Response to Rejection Under 35 U.S.C. § 102 as anticipated by Holmes

Currently pending Claims 1-16 are rejected under 35 U.S.C. § 102 (b) as being anticipated by Holmes *et al.* (U.S. Patent No 5,679,773) ("Holmes"). The Examiner maintains that Holmes discloses compounds synthesized on solid supports, which may be released upon completion of synthesis.

Indeed, Holmes teaches methods for solid phase synthesis of organic molecules. Holmes discloses reagents having attached linking groups which are useful in solid phase syntheses of high density arrays of organic molecules. Holmes, however, does not teach pooling. Note that while Holmes discloses cleaving a labeled polymer for quality control analysis (col. 22, lines 16-25), they do not teach cleaving first and second linkers to produce a pool of oligonucleotides.

In contrast, the present invention provides methods for generating a pool of oligonucleotides. The method comprises providing a substrate and at least first and second different oligonucleotides linked to the substrate through first and second cleavable linkers, respectively; and cleaving the first and second linkers, thereby releasing the first and second oligonucleotides from the substrate thereby generating a pool of oligonucleotides comprising the first and second oligonucleotides. The invention finds use in preparing a pool of oligonucleotides in solution for a variety of nucleic acid detection and/or amplification assays.

As the Examiner is aware, anticipation under 35 U.S.C. § 102 requires that "[f]or a prior art reference to anticipate in terms of 35 U.S.C. § 102, every element of the claimed invention must be identically shown in a single reference." In re Bond, 15 USPQ2d 1566, 1567 (Fed. Cir. 1990).

Here, Holmes does not teach providing a substrate and at least first and second different oligonucleotides linked to the substrate through first and second cleavable linkers, respectively; and cleaving the first and second linkers, thereby releasing the first and second oligonucleotides from the substrate thereby generating a pool of oligonucleotides comprising the first and second oligonucleotides. Holmes is directed

to methods of synthesizing compounds on, for example an array, which may be released, however, nowhere in the patent is "pooling" or a "pool" of oligonucleotides mentioned. Moreover, nowhere does the patent teach cleaving first and second linkers.

Accordingly, Applicants submit that every element of the claimed invention is not shown in the sited reference, and thus claims 1-16 are not anticipated by Holmes. Applicants respectfully request the Examiner to withdraw the rejection.

CONCLUSION

Applicants submit that the claims as amended are in form for immediate allowance and the Examiner is respectfully requested to early notification to that effect.

The Examiner is invited to contact the undersigned at (415) 781-1989 if any issues may be resolved in that manner.

Respectfully submitted,
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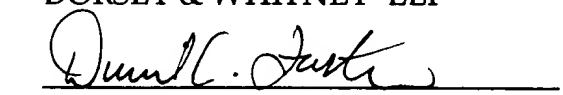

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Appendix A

COPY OF THE PENDING CLAIMS

1. A method of generating a pool of oligonucleotides comprising:
a) providing a substrate and at least first and second different oligonucleotides linked to said substrate through first and second cleavable linkers, respectively; and
b) cleaving said first and second linkers, thereby releasing said first and second oligonucleotides from said substrate thereby generating a pool of oligonucleotides comprising said first and second oligonucleotides.

2. A method according to claim 1, wherein said first and second oligonucleotides comprise oligonucleotides of known sequence.

3. A method according to claim 1, wherein said first and second oligonucleotides are labeled.

4. (Amended) A method according to claim 3, wherein said first and second oligonucleotides bear different labels.

5. A method according to claim 3, wherein said first and second oligonucleotides are attached covalently through said first and second linkers, respectively, to said substrate.

6. A method according to claim 3, wherein said first and second oligonucleotides are synthesized on said substrate.

7. A method according to claim 1, wherein said substrate comprises discrete sites to which said first and second oligonucleotides may be linked.

8. A method according to claim 7, wherein said first and second oligonucleotides are immobilized to first and second beads through said first and second linkers, respectively, and wherein said first and second beads are distributed at said discrete sites.

9. A method according to claim 1, further comprising synthesizing said first and second oligonucleotides on said substrate.

10. The method according to claim 9, wherein said first and second oligonucleotides are synthesized by a synthesis method selected from the group consisting of printing and photolithography.

11. A method for generating a pool of oligonucleotides, said method comprising:
a) providing an array comprising a substrate and a population of

oligonucleotides, said population comprising at least first and second subpopulations comprising at least first and second different oligonucleotides, respectively, said first and second oligonucleotides being immobilized to first and second beads, respectively, through first and second cleavable linkers, respectively, said first and second beads being distributed on said substrate; and

b) cleaving said first and second linkers, thereby releasing said first and second subpopulations from said first and second beads, thereby generating a pool of oligonucleotides comprising said first and second oligonucleotides.

12. A method according to claim 11, wherein said first and second oligonucleotides comprise known sequence.

13. A method according to claim 11, wherein said first and second oligonucleotides are labeled.

14. A method according to claim 13, wherein said first and second oligonucleotides are labeled with different first and second labels, respectively.

15. A method for generating a pool of oligonucleotides, said method comprising:

a) providing an array comprising a substrate and a population of oligonucleotides, said population comprising at least first and second subpopulations comprising at least first and second different oligonucleotides of known sequence, said first and second oligonucleotides being immobilized directly to a chip through first and second cleavable linkers, respectively; and

b) cleaving said first and second linkers, thereby releasing said first and second subpopulations from said chip, thereby generating a pool of oligonucleotides comprising said first and second oligonucleotides.

16. The method according to claim 15, wherein said first and second oligonucleotides are labeled.

Appendix B

MARKED UP VERSION OF THE CLAIMS

4. (Amended) A method according to claim 3, wherein said first and second [different] oligonucleotides bear different labels.